

## EXHIBIT 21

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**Expression of deoxycytidine kinase in leukaemic cells compared with solid tumour cell lines, liver metastases and normal liver.**

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Deoxycytidine kinase (dCK) is required for the phosphorylation of several deoxyribonucleoside analogues that are widely employed as chemotherapeutic agents. Examples include cytosine arabinoside (Ara-C) and 2-chlorodeoxyadenosine (CdA) in the treatment of acute myeloid leukaemia (AML) and gemcitabine to treat solid tumours. In this study, expression of dCK mRNA was measured by a competitive template reverse transcriptase polymerase chain reaction (CT RT-PCR) in seven cell lines of different histological origin, 16 childhood and adult AML samples, 10 human liver samples and 11 human liver metastases of colorectal cancer origin. The enzyme activity and protein expression levels of dCK in the cell lines were closely related to the mRNA expression levels ( $r=0.75$ ,  $P=0.026$  and  $r=0.86$ ,  $P=0.007$ ). In AML samples, dCK mRNA expression ranged from 1.16 to 35.25 ( $\times 10^{-3}$ )xdCK/beta-actin). In the cell line panel, the range was 2.97-56.9 ( $\times 10^{-3}$ )xdCK/beta-actin) of dCK mRNA expression. The enzyme activity in liver metastases was correlated to dCK mRNA expression ( $r=0.497$ ,  $P=0.05$ ). In the liver samples, these were not correlated. dCK mRNA expression showed only a 36-fold range in liver while a 150-fold range was observed in the liver metastases. In addition, dCK activity and mean mRNA levels were 2.5-fold higher in the metastases than in the liver samples. Since dCK is associated with the sensitivity to deoxynucleoside analogues and because of the good correlation between the different dCK measurements in malignant cells and tumours, the CT-RT PCR assay will be useful in the selection of patients that can be treated with deoxycytidine analogues.

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